

RemarksResponse to Item V of Written OpinionNovelty and Inventive Step

Claims 1-25 are indicated as lacking novelty over U.S. Patent 6,117,674. Claims 1, 13 and 23 have been amended to more particularly indicate an aspect of the present invention. Support for the claim amendments can be found at pages 12-13. Claims 1, 13 and 23 now recite that the infection of the tissue mass with a pathogen or treatment of the tissue mass with a toxin, takes place after the tissue mass has been removed from the bioreactor vessel and seeded into a tissue culture vessel, *i.e.*, outside of the bioreactor vessel.

In addition, although the '674 patent teaches the infection of the tissue culture within the bioreactor vessel, the reference does not discuss the manipulation of the formed tissue mass outside of the bioreactor environment. In addition, the purpose of the invention disclosed in the '674 patent is to promote pathogen propagation and growth and production of pathogenic products. See '674 patent at col. 9, lines 10-12. On the other hand, the purpose of the present invention is to study the infectivity of a pathogen or the chemosensitivity of a toxin within a tissue mass.

In sum, the invention disclosed in the '674 patent differs from the present invention in at least two respects. Firstly, in the present invention, the tissue mass is infected with a pathogen or treated with a toxin outside the bioreactor vessel, whereas the '674 patent teaches the pathogen infection of the tissue mass inside the bioreactor vessel. Secondly, the invention in the '674 patent pertains to the propagation of a pathogen within a tissue mass, whereas the present invention pertains to studies of the infectivity of a pathogen within a tissue mass and chemosensitivity of a formed tissue mass to a particular toxin.

Conclusion

Applicants believe that the amended claims as presented provide novelty and inventive step over the cited reference. Therefore, an International Preliminary Examination Report stating that the claims as amended possess both novelty and inventive step is earnestly requested.

**Marked-up Version of Amended Claims**

1. (Amended) A method of studying the infectivity of a pathogen in tissues comprising the steps of:

- isolating host cells;
- placing said isolated host cells into a bioreactor comprising culture medium;
- applying sedimental shear stress to the cells in the cell culture to form a three-dimensional tissue mass;
- seeding the formed tissue mass in a tissue culture vessel;
- introducing an infectious pathogen into [said culture containing] said three-dimensional tissue mass; and
- assaying the infectivity of said infectious pathogen.

13. (Amended) A method of measuring the chemosensitivity of tissues to a toxic materials comprising:

- isolating host cells;
- placing said isolated host cells into a bioreactor comprising culture medium;
- applying sedimental shear stress to the cells in the cell culture to form a three-dimensional tissue mass;
- seeding the formed tissue mass in a tissue culture vessel;
- introducing a toxic material into [said culture containing] said three-dimensional tissue mass; and
- assaying the chemosensitivity of said toxic material.

23. (Amended) A method of measuring the chemosensitivity of tissues to a toxic materials comprising:

- isolating human renal epithelial cells;
- placing said isolated human renal epithelial cells into a bioreactor comprising culture medium;
- applying sedimental shear stress to the cells in the cell culture to form a three-dimensional tissue mass;
- seeding the formed tissue mass in a tissue culture vessel;
- treating the three dimensional tissue mass with a toxic material; and
- assaying the chemosensitivity of said toxic material.